of 11 (73%) patients indicated that shocks ≤ 1 J were painful and all required sedation at a shock energy level > 2 J.

Conclusions: (1) Internal atrial defibrillation could be safely and effectively performed in all patients in this series. (2) However, only in 36% of the patients atrial fibrillation could be terminated with an energy ≤ 3 J. Thus, only a minority of patients may benefit from an implantable atrial defibrillator capable of storing a maximum shock energy of 3 J. (3) Pain perception may have a major impact on quality of life in patients with an implantable atrial defibrillator since the majority of the patients (73%) reported severe pain at shock energies < 1 J.

11:30

789-5 Safety of Transvenous Atrial Defibrillation in Patients With Monomorphic Ventricular Tachycardia and Heart Disease

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History of ventricular tachycardia (VT) and depressed ejection fraction may affect transvenous atrial defibrillation (AD) increasing the likelihood of shock-related arrhythmias. In 25 pts with VT (mean age 65 ± 8 years; EF 29 ± 9%) we assessed the safety of AD using 2 catheters in the right atrial appendage and coronary sinus. In each pt, AD was performed with increasing energy starting at 0.5 joules. The protocol was performed both in drug free state and during isoproterenol infusion. In 5 pts AD was attempted during VT and atrial pacing with AV conduction at the same rate of VT. Shocks were synchronized using a Medtronic external defibrillator model 2394. A total of 398 shocks were analyzed. No ventricular tachyarrhythmias were observed after shocks synchronized on the R wave. In 3 pts ventricular fibrillation followed inappropriate shocks on the T wave. In all 3 pts, T wave shocking was seen only during isoproterenol infusion. Shocks delivered during VT always resulted in acceleration of VT (1 pt) or degeneration to VF (4 pts). However in the same pts shocks during atrial pacing with ventricular rate similar to VT did not induce ventricular arrhythmias. In conclusion: 1) In pts with VT transvenous atrial defibrillation is safe when shocks are properly synchronized. 2) Atrial defibrillation during VT appears proarrhythmic. 3) Whether isoproterenol infusion increases the likelihood of inappropriate T wave oversensing needs further evaluation.

11:45

789-6 Repeated Internal Low-Energy Cardioversion of Atrial Fibrillation

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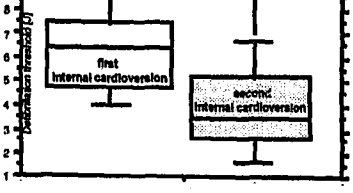
Background: The goal of this study was to determine if repeated internal cardioversion (intCV) of atrial fibrillation (AF) required the same energy for conversion as previous successful intCVs.

Methods: IntCV was successfully performed in 51 of 56 pts by delivering 3 ms/2 ms biphasic shocks (Ventritex HVS 02, Sunnyvale CA) between two custom-made intracardiac electrode catheters (6F, Elecath Inc., Rahway NJ). The shocks were R-wave triggered, voltage was increased by 40V per shock in intervals until sinus rhythm was achieved. Pts were sedated with Midazolam. After a mean follow-up of 11 ± 6 months, 20 pts experienced a second episode of AF. In 8 of these pts (age 59 ± 10 years, initial episode AF persisting for 7.1 ± 2.5 months, with a mean left atrial echocardiographic diameter of 56.6 ± 2.4 mm) intCV was attempted a second time after a mean AF relapse duration of 1.3 ± 0.9 months.

Results: Sinus rhythm was restored with a mean energy of 6.4 ± 2.1 J (range 1.0–10.2 J) in the first and 3.8 ± 1.7 J in the second intCV ($p < 0.05$) in all 8 pts.



Conclusions: Repeat intCV requires less energy than primary intCV of chronic AF given that the second episode is of shorter duration than the first. A large number of pts are ineligible for atrial defibrillator implantation due to atrial defibrillation thresholds (DFTs) exceeding the acceptable pain level. This study implies that such pts would have considerably lower DFTs, and as a result less pain, if their AF was quickly detected and addressed, such as in the case of an implanted atrial defibrillator. Therefore, these pts may indeed be suitable candidates for atrial defibrillator implantation.

790 Nitric Oxide: Physiology, Pharmacology, and Pathology

Wednesday, March 27, 1996, 10:30 a.m.–Noon
Orange County Convention Center, Room 208

10:30

790-1 In Vivo Nitrate Tolerance Is Not Associated With Decreased Production of Nitric Oxide

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Reduced bioconversion of nitroglycerin (NTG) to nitric oxide (NO) is regarded as a major contributor to the development of nitrate tolerance (Tol). However, the validity of this hypothesis has not been examined. We measured production of NO in vascular tissues from nitrate tolerant and non-tolerant rats by in vivo spin-trapping of NO. Conscious rats received an i.v. infusion of NTG (1 mg/hr, Tol + NTG group, (n = 8)) or NTG vehicle. (placebo + NTG group, (n = 8)) for 72 hrs and NO was trapped by diethyldithiocarbamate (DETC) and Fe^{2+}-citrate during an additional final 20-min infusion of NTG (6.5 mg/kg). Baseline NO production was measured in another group of rats not treated with NTG (n = 8, control). Tolerance was documented after 72 h. by an 83% reduction in the hypotensive response to a NTG bolus (From 24 ± 3 (0 hrs) to 2 ± 1 mmHg (72 hrs); $p < 0.05$). Tissues were removed and analyzed for $NOFe(DETC)_2^2$ complexes by ESR spectroscopy. Data are presented as nmol NO/g tissue/20 min.

Mean (± Sem)	Aorta	V. cava	Heart	NTG Responses (mm Hg)
Tol + NTG	1.8 ± 0.3	2.2 ± 0.3	5.1 ± 0.5	24 ± 3 vs 2 ± 1
Placebo + NTG	0.9 ± 0.2	1.2 ± 0.2	1.7 ± 0.2	25 ± 3 vs 2 ± 1
Control	0 ± 0	0 ± 0	0.2 ± 0.01	27 ± 3

The results suggest that the amounts of NO produced from NTG in hemodynamically nitrate tolerant rats (TOL ± NTG) are higher or similar to the amounts of NO produced in non tolerant rats (placebo + NTG, $p < 0.05$). It is concluded that the in vivo NTG tolerance is not caused by a reduced bioconversion of NTG to NO. Instead, tolerance may be associated with a reduction of the biological activity of NO.

10:45

790-2 Antiplatelet Effect of Nitroglycerin Is Primarily Mediated by Glutathione-s-Transferases in Human Plasma

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Current hypothesis relative to the mechanism of action of NTG involves metabolic activation of NTG to nitric oxide (NO) by glutathione-s-transferases (GST). Whereas GST metabolizes organic nitrates in the liver, it is unclear if these enzymes are present in human plasma or platelets, and are involved in the antiplatelet effects of NTG. We investigated the role of GST in the inhibition of platelet aggregation by NTG. Different concentrations of NTG (1–100 μg/ml) were incubated with platelet-rich plasma or washed platelet suspension, and aggregation induced by ADP or thrombin. NTG caused a concentration-dependent inhibition of platelet aggregation in platelet-rich plasma with $IC_{50} \approx 50$ μg/ml. The aggregation inhibitory effect of NTG was not observed in washed platelet suspension. In contrast, authentic NO caused about 50% decrease in aggregation in washed platelet suspension. The aggregation inhibitory effect of NTG in platelet-rich plasma was oxyhemoglobin (Hb)-sensitive. The aggregation inhibitory effect of NTG in platelet-rich plasma was potentiated by propylthiouracil (600 μg/ml), a GST inducer, and antagonized by ketoprofen (100 μg/ml), a GST inhibitor. These phenomena were not observed in washed platelet suspension. Since Hb cannot penetrate platelets, reversal of the effect of NTG by Hb must have been due to removal of NO from the extracellular medium. This concept was confirmed in other studies, wherein NTG (100 μg/ml) increased nitrite levels 3 fold in platelet-rich plasma after 60 min incubation. On the other